

A CANTILEVER SENSOR USING BOTH THE LONGITUDINAL AND THE TRANSVERSAL
PIEZORESISTIVE COEFFICIENTS

Field of the invention

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The present invention relates to a sensor comprising one or more sensor units, wherein each sensor units comprises a capture surface area and a piezoresistive detection system, for direct detection of stress change
10 of the sensor unit. One type - the most commonly used type of sensor unit - is a cantilever.

The invention also relates to a method of producing such sensor.

15

Background of the invention

In the art of detecting components in fluids, cantilever based sensors with integrated piezoresistors are used as very sensitive mechanical stress sensors. As described
20 in e.g. WO 0066266 and WO 9938007, micro cantilevers can be used for detection of molecular interaction. At least one surface of the cantilever is coated with a capture layer, which capture layer reacts with a target molecule of interest. If the cantilever is exposed to a sample in
25 which the target molecule is present, the target molecule will react with the capture molecule on the cantilever surface and a surface stress change will be generated.

30 Due to the surface stress change of the cantilever, a mechanical compression, stretch or decompression is applied to the cantilever and thereby also to the piezoresistor, and thereby the resistivity of the piezoresistor changes its value. The mechanical

compression or decompression may result in a deflection and/or a stretch and/or a contraction. By measuring the change in resistance, it can be determined whether the target molecule is present in the sample or not, and if
5 so it may also be possible to detect the concentration of the target molecule.

Cantilever-based sensors with integrated piezoresistive read-out are described by Thaysen, Ph.D.
10 Thesis, "Cantilever for Bio-Chemical Sensing Integrated in a Microliquid Handling System", September 2001, Microelektronik Centeret, Technical University of Denmark. Hereby the stress changes on the cantilever sensors can be measured directly by the piezoresistor.
15 Moreover, integrated read-out greatly facilitates operation in solutions since the refractive indices of the fluids do not influence the detection as it will using optical read-out. Each sensor may have a built-in reference cantilever, which makes it possible to
20 subtract background drift directly in the measurement. Furthermore, by functionalizing the reference cantilever with a "dummy" molecule, non-specific binding events occurring on both the measurement and reference cantilever will be cancelled out in the differential
25 measurement.

The two cantilevers may be connected in a Wheatstone bridge, and the stress change on the measurement cantilever is detected as the output voltage from the
30 Wheatstone Reference is also made to "Design issues in SOI-based high-sensitivity piezoresistive cantilever devices" by Kassegne et al. Proceedings of the SPIE Conference on Smart Structures and Materials, San Diego, CA, March 17-21 2002.

The objective of the present invention is to provide a sensor comprising one or more sensor units with a capture surface, which sensor can be used for detection
5 of the presence of a target in a fluid, such as a chemical component in a liquid or a gas e.g. for detecting an explosive, a drug, a biocomponent or other components in a fluid with an improved signal or signal/noise ratio than according to the prior art
10 cantilevered fluid sensors.

This and other objectives as it will be clear from the following description, has been solved by the invention as it is defined in the claims.

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Disclosure of the invention

The sensor of the invention comprises one or more sensor units. The shape and size of the sensor and the size,
20 shape and the number of sensor units as well as its wiring, may e.g. be as disclosed in any one of the patent applications WO 0066266, DK PA 2001 01724 DK PA 2002 00283, DK PA 2002 00125 and DK PA 2002 00195, which with respect to the disclosure concerning structure
25 (shape and size of the sensor and the size, shape and the number of sensor units as well as its wiring) are hereby incorporated by reference.

In the following the sensor is described with one sensor
30 unit, only, but it should be understood that the sensor unit may have several sensor units, such as up to 300, e.g. up to 100.

- The sensor unit may in principle have any cantileverlike shape e.g. as the cantilevers described in DK PA 2002 00125. The term 'cantilever shape' is defined as a sheet formed unit linked to a substrate (or two substrates) along one or two opposite edge lines. The term 'cantilever shape' thus also includes a bridge, as well as a traditional rectangular, triangular or leaf shaped cantilever.
- 10 In one embodiment, the sensor unit shaped as a cantilever extending in a length between two endings and linked in both of its endings to form a cantilevered bridge.
- 15 In another embodiment, the cantilever is a traditional rectangular or leaf shaped cantilever linked to one substrate only. In the following this type of cantilevers are referred to as cantilevers with a free end.
- 20 The sensor unit comprises two major surfaces, wherein one or both of these totally or partly may constitute a capture surface.
- 25 In one embodiment the sensor unit is a flexible sheet-formed unit having an average thickness which is thinner than both its average length and its average width, said sensor unit preferably have a thickness of between 0.05 and 5 μm , such as in the interval of 0.1 μm to 4 μm ,
30 such as in the interval of 0.2 μm to 1 μm .

In one embodiment the sensor unit is a flexible sheet-formed unit having an average thickness which is at least

5 times, preferably at least 50 times less than its average width and average length.

The sensor unit has a capture surface e.g. in the form of a capture coating. The capture coating may e.g. be as described in any one of the applications DK PA 2002 00283 and DK PA 2002 00125 or in US 6289717, WO 0133226 or WO 0014539, which with respect to the disclosure concerning the capture surface are hereby incorporated by reference.

10 In one embodiment of the sensor according to the invention, the capture surface is a surface of a capture coating comprising a capture layer, wherein said capture layer is a layer comprising a detection ligand, said
15 detection ligand may be a member of a specific binding pair or it may be adapted for capturing a group of components or even for unspecific binding. The detection ligand is preferably selected from the group consisting of RNA oligos, DNA oligos, PNA oligos, proteins,
20 enzymes, receptors, peptides, hormones, blood components, antigen and antibodies.

In one embodiment of the sensor according to the invention, the capture surface is a surface of a capture
25 coating comprising a capture layer, of polymer, hydrogel or metal/metal containing component e.g. comprising a functional group selected from the group consisting of carboxylic acids, sulfonic acid derivatives, esters, acid halides, acid hydrazides, semicarbazides,
30 thiosemicarboxides, nitriles, aldehydes, ketones, alcohols, thiols, disulphides, amines, hydrazines, ethers, epoxides, sulphides, halides and derivatives thereof.

The capture coating could in principle have any thickness. If the capture coating is very thick the sensitivity may be reduced due to stiffness of sensor unit. A desired thickness could e.g. be from molecular
5 thickness to 2000 nm, such as up to, 2, 5, 10 or 50 molecule layers, or e.g. between 0.5 nm and 1000 nm, such as between 1 and 500 nm, such as between 10 and 200 nm.

- 10 In one embodiment both or a part of both of the two major sides of the cantilever comprise a capture surface. The capture surfaces may be identical or they may differ from each other e.g. with respect to size of area covered, type of capture molecules and/or concentrations thereof.
- 15 In one embodiment the capture surface on one major side of a cantilever is essentially identical, - both with respect to size of area covered, type of capture molecules and concentrations - to the capture surface on the other one of the two opposite major surfaces of the
- 20 cantilever. In this situation the stress generated on the cantilever when subjected to a fluid containing the target molecules, will be equal on both sides of the cantilever, and consequently, if the cantilever is of the type with a free end, the cantilever will not bend, but
- 25 only stretch or contract.

In practice it is very cumbersome to produce a cantilever with two opposite major sides with identical capture surfaces. Thus, the cantilever will in most situations,
30 even when carrying capture surfaces on both of each major sides, be subjected to at least a slightly bending due to different stress generated on the opposite major sides of the cantilever.

The sensor unit comprises a piezoresistive element with a pair of wires for applying an electrical field over the piezoresistive element. The distance between the wires along the piezoresistive element is defined as the
5 length of the piezoresistive element. This means in practice that the length of the piezoresistive element is the length that the current has to travel through the piezoresistive element. In one embodiment the length of the piezoresistive element is thus defined as the length
10 the current has to travel.

The piezoresistor may have any shape e.g. as described in any one of the patent applications WO 0066266, DK PA 01724 DK PA 2002 00283, DK PA 2002 00125 and DK PA 2002
15 00195. The piezoresistive element may e.g. be, latter shaped, meander shaped, U shaped or V shaped.

In practice it is most simple to either provide the piezoresistive element as a straight element when the
20 cantilever is linked to be a bridge or provide the piezoresistive element as a horse shoe shape when the cantilever has a free end.

The piezoresistive element has a longitudinal direction and a transverse direction along the length of the
25 piezoresistive element when an electrical field is applied over the piezoresistive element and the piezoresistive element is subjected to a stress. The longitudinal direction and the transverse direction may
30 vary along the length of the piezoresistive element if the piezoresistive element is not straight.

The coordinate system may in principle be aligned as desired provided that the longitudinal direction is

defined as a direction which is one of the x, y or z axis of a coordinate system and wherein there is a stress composant and a current composant. The resulting numerically value of the sum of the longitudinal
5 piezoresistive coefficient π_l and the transverse piezoresistive coefficient π_t can thereby be detected.

In one embodiment for simple calculation the coordinate system should preferably be aligned so that only one
10 direction for a given point along the length of the piezoresistive element qualifies as a longitudinal direction.

In one embodiment the coordinate system is aligned to
15 the crystal axis.

The most simple calculation is provided when the coordinate system is aligned so that the direction of the current through the piezoresistive element is the
20 longitudinal direction. This system is used below in the examples.

The transverse direction is perpendicular to the longitudinal direction. In one embodiment the transverse
25 direction also has a stress composant.

If we consider the surface stress of a local point of the sensor piezoresistive element, the sensor will in principle bend a a cup in all directions if no other
30 forces are involved. The piezoresistive element is thus stressed in all directions in this point, and this stress is divided into two stress composant a longitudinal and a transversal. For simple calculation

the longitudinal stress component is in the direction of the current.

Further information concerning determination of longitudinal and transversal direction in a silicon piezoresistive element can be found in "Classification and terminology of sensors, S. M. SZE, Semiconductor Sensors, ISBN 0-471-54609-7, 1994, John Wiley & Sons Inc. pages 160-169 which is hereby incorporated by reference.

In one embodiment, the piezoresistive element is a straight element, the piezoresistive element has only one longitudinal and transverse directions along its length. In another embodiment, the piezoresistive element is shaped as a horse shoe, the piezoresistive element has two longitudinal and transverse directions along its length.

The piezoresistive element is of an anisotropic material, is being arranged so that the numerically value of the sum of the longitudinal piezoresistive coefficient π_l and the transverse piezoresistive coefficient π_t along at least 25 % of the length, such as at least along 50 % of the length such as at least along 80 % of the length, such as at least along 90 % of the length, such as at least along 95 % of the length of the piezoresistive element being at least $10^{-10}\text{Pa}^{-1} \times P$, such as $2 \times 10^{-10}\text{Pa}^{-1} \times P$, such as $3 \times 10^{-10}\text{Pa}^{-1} \times P$, such as $4 \times 10^{-10}\text{Pa}^{-1} \times P$, wherein P is the piezoresistance factor, and wherein the piezoresistive coefficients π_l and π_t are determined as components in the coordinate system used to determine the longitudinal direction.

In one embodiment the numerically value of the sum of the longitudinal piezoresistive coefficient π_l and the transverse piezoresistive coefficient π_t along the whole of its length is at least $10^{-10}\text{Pa}^{-1} \times P$, such as $2 \times 10^{-10}\text{Pa}^{-1} \times P$, such as $3 \times 10^{-10}\text{Pa}^{-1} \times P$, such as $4 \times 10^{-10}\text{Pa}^{-1} \times P$.

The piezoresistance factor P is depending on the doping level. P is between 0 and 1. For single crystalline silicon P is about 1 at a doping level around 10^{18} . Further information concerning the P factor and the determination thereof can be found in "1/F Noise Considerations for the Design and Process Optimization of Piezoresistive Cantilevers" by Jonah A. Harley and Thomas W. Kenny. Journal of microelectromechanical systems. Vol, 9, No. 2, pp 226-235. June 2000. Reference is in particular made to figure 7. Reference is also made to Y. Kanda. "A graphical representation of the piezoresistance coefficients in silicon" IEEE Trans. Electron Devices, Vol. ED-29, pp 64-70, Jan. 1982.

A piezoresistive effect in a material indicates the fractional change in bulk resistivity induced by a small mechanical stress applied to the material. Single crystalline silicon has a high piezoresistivity, and combined with its excellent mechanical and electronic properties, it makes it a useful material for the conversion of a mechanical signal into an electrical signal.

The piezoresistive element may therefore preferably be of doped single crystalline silicon. In one embodiment

the piezoresistive element is of single crystalline silicon doped with 10^{16} ions/cm³ or more, such as 10^{17} ions/cm³ or more, such as 10^{18} ions/cm³ or more, such as 10^{19} ions/cm³ or more, such as 10^{20} ions/cm³ or more.

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In one embodiment the piezoresistive element is of single crystalline silicon doped with 10^{20} ions/cm³ or less, such as 10^{19} ions/cm³ or less, such as 10^{18} ions/cm³ or less, such as 10^{17} ions/cm³ or less.

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The higher level of doping ions the lower is the amount of noise, however simultaneously the signal will also be reduced accordingly. The temperature may also influence the noise as well as the signal, and accordingly the effect of temperature should also be considered. The optimal doping level can easily be found by the skilled person based on the present teaching. Optimal doping level will be in the interval 10^{16} ions/cm³ - 10^{21} ions/cm³.

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In one embodiment the surplus or shortage of electrons due to the doping is within the interval 10^{16} ions/cm³ - 10^{21} ions/cm³.

25 The doping ions may in principle be any type of ions usable for doping silicon or mixtures of ions. In one embodiment, when n-type and p-type ions are mixed, it is desired that the piezoresistive element comprise at least 10^{16} ions/cm³, such as 10^{17} ions/cm³ or more, such as
30 10^{18} ions/cm³ or more, such as 10^{19} ions/cm³ or more, such as 10^{20} ions/cm³ or more, more of one of the types than of the other one of the types.

In one embodiment, the piezoresistive element being of single crystalline silicon doped with one or more of the ions boron ion, phosphorous ion, arsenic ion.

5 In one embodiment the piezoresistive element is n-type single crystalline silicon. The n-type single crystalline silicon may e.g. be orientated along the <110> direction of silicon. In another embodiment the n-type silicon piezoresistive element is orientated along
10 the <100> direction of silicon.

The thickness of the piezoresistive element may e.g. be at least 10 nm, such as in the interval of 10 nm to 500 nm, such as in the interval of 50 nm to 300 nm, such as
15 in the interval of 100 nm to 200 nm.

As mentioned, the sensor unit also comprise a pair of wires for applying an electrical field over the piezoresistor, e.g. as described in any one of the patent
20 applications WO 0066266, DK PA 01724 DK PA 2002 00283, DK PA 2002 00125 and DK PA 2002 00195.

In one embodiment of the sensor according to the invention, where the sensor unit comprises two major
25 surfaces, and at least a part of one or both of the major surfaces constitutes the capture surface, the piezoresistive element has a neutral plan distance of 50 nm or less, such as 100 nm or less, such as 200 nm or less, such as 400 nm or less, such as 1 μ m or less, such
30 as 3 μ m or less,. The neutral plan distance is measured as the shortest distance between the middle plan of the piezoresistive element and the neutral plan. The middle plan of the piezoresistive element is defined as the middle plan through the piezoresistive element which is

parallel to the neutral plan. The neutral plan is defined as the plan along which the sum of the compressive and tensile stress acting on the piezoresistive element is as close to zero as possible.

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In one embodiment, the sensor unit further comprise a current shield, e.g. as described in DK PA 2002 00884 DK filed June 7, 2002.

- 10 The shield may have a diffusion barrier which is sufficient to prevent the diffusion of an electrolyte to leak current from the piezoresistor when an acidic liquid at a pH of 4 is held in contact with the capture surface for a period of 1 or even 2 minutes or even 10 minutes
15 under standard conditions.

In one embodiment the shield is of a non-conducting material selected from the group consisting of nitrides, such as silicon nitride and tantalum nitride, non-
20 conducting polymers, such as octafunctional epoxidized novalac, metal oxides, such as aluminium oxide, ceramics, diamond films, silicon carbide, tantalum oxide, silicon, glass, mixtures and combinations thereof.

- 25 In one embodiment the piezoresistive element is of doped n-type single crystalline silicon and the shield is of doped p-type single crystalline silicon, preferably a p-type single crystalline silicon with a doping level which is lower than the doping level of the n-type single
30 crystalline silicon piezoresistive element. The p-type single crystalline silicon shield may e.g. have a doping ion concentration of 10^{20} cm^{-3} or less, such as a doping ion concentration of 10^{19} cm^{-3} or less, such as a doping ion concentration of 10^{18} cm^{-3} or less, such as a doping

ion concentration of 10^{17} cm^{-3} or less, such as a doping ion concentration of 10^{16} cm^{-3} or less, such as a doping ion concentration of 10^{15} cm^{-3} or less.

- 5 In one embodiment the sensor unit comprise a bottom shield layer and a top shield layer, and an edge shield layer. The bottom shield layer, top shield layer and edge shield layer constitute the shield.
- 10 A sensor wherein the sensor units comprise a shield may preferably be used for detection of a substance in a liquid, such as an aqueous liquid.

The sensor may preferably comprise one or more fluid chambers (e.g. liquid chambers). In one embodiment the one or more sensor units partly or totally protrudes into the fluid chamber(s) so that a fluid applied in the chamber is capable of coming into contact with part of the surface of the sensor unit(s).

20 The fluid chamber or chambers may e.g. be in the form of interaction chamber(s), preferably comprising a channel for feeding a fluid such as a liquid into the interaction chamber(s).

25 In one embodiment at least 50 %, more preferably substantially all of the capture surface of the sensor unit or units is positioned inside the fluid interaction chamber(s).

30 The sensor may e.g. be prepared as described in DK PA 2002 00884 DK with the difference that the doping may be an n-type doping and that the single crystalline silicon piezoresistive element is arranged so that the

numerically value of the sum of the longitudinal piezoresistive coefficient π_l and the transverse piezoresistive coefficient π_t along the major length, such as at least along 25 % of the length, such as at least along 50 % of the length, such as at least along 60 % of the length, such as at least along 80 % of the length, such as at least along 90 % of the length, such as at least along 95 % of the length of the piezoresistive element being at least $10^{-10}\text{Pa}^{-1} \times P$, such as $2 \times 10^{-10}\text{Pa}^{-1} \times P$, such as $3 \times 10^{-10}\text{Pa}^{-1} \times P$, such as $4 \times 10^{-10}\text{Pa}^{-1} \times P$.

Figures and examples

Embodiments of the invention will be described further with reference to the figures and examples.

Figure 1 shows the piezoresistive coefficients for π_l and π_t for p-type (A) and n-type (B) silicon. (At room temperature, in 10^{-11}Pa^{-1}).

Figure 2 shows a Wheatstone bridge for converting the relative change in resistance from the measurement cantilever into a change in voltage.

Figure 3, shows a change in signal due to immobilization of 1mM Mercaptohexanol for respectively a sensor unit with an n-type piezoresistive element and a sensor unit with a p-type piezoresistive element. It can be seen that the signal from the n-type cantilever is about a factor of 8 larger than the signal obtained from the p-type piezoresistive cantilever. Note that the change in output voltage for the n-type piezoresistive cantilever

is negative compared to the p-type piezoresistive cantilever.

Figure 4 is a schematic illustration of a cantilever.

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Figure 5 shows a cantilever with a stressed surface.

The piezoresistivity in single crystalline silicon is anisotropic and therefore the sensitivity is also dependent on the piezoresistor orientation with respect to the silicon crystalline. According to the invention it has been found that the contribution to the relative resistance changes from stress generated on a cantilever surface is given by:

15

$$\frac{\Delta R}{R} = \sigma_l \pi_l + \sigma_t \pi_t \quad (1)$$

where σ_l and σ_t is the longitudinal and transverse stress respectively, while π_l and π_t indicates the piezoresistive coefficients. For p-type/n-type silicon wafer with (100) plane at the surface of the wafer the piezoresistive coefficients at room temperature (in 10^{-11} Pa^{-1}) and doping level about 10^{18} cm^{-3} (p is approximately 1) is given in table 1.

25

	Direct ion	π_{11}	π_{12}	π_{44}	π_t	π_l
p-Si	<100>				0	0
	<110>	6.6	-1.1	138.1	-66	72
n-Si	<100>				53	-102
	<110>	-102.2	53.4	-13.6	-18	-31

Table 1

The longitudinal piezoresistive coefficient in the $\langle 110 \rangle$
5 direction is determined as

$$\pi_l = 1/2 (\pi_{11} + \pi_{12} + \pi_{44}),$$

and the corresponding transverse coefficient is
10

$$\pi_t = 1/2 (\pi_{11} + \pi_{12} - \pi_{44}).$$

Figure 1 shows the piezoresistive coefficients for π_l and
15 π_t for p-type (A) and n-type (B) silicon. It is seen that
the n-type piezoresistive coefficients are much more
non-symmetrical than the p-type coefficients.

When a cantilever with integrated piezoresistor is used
20 as a longitudinally deflection sensor only, the
piezoresistor is placed such that only the longitudinal
stress is picked up. Since the cantilevers are usually
released by a wet etch, such as KOH, the cantilever may
e.g. be aligned to the substrate such that a good
25 clamping is obtained. Usually, the wet etch is
anisotropically and etches the $\langle 111 \rangle$ direction much
slower than the other directions. Since the intersection
of the $\{111\}$ plane and the $\{100\}$ plane are lying along
the $\langle 110 \rangle$ orientations, it has been found desired to
30 align the cantilever in the $\langle 110 \rangle$ direction in order to
release it with a good clamping.

According to the invention it has been found that the surface stress generated on a sensor unit comprising a capture surface, introduces a constant curvature or stretch or contraction at the areas where the surface stress is applied and no bending at places the surface stress is not applied. In areas adjacent a clamping line the bending in the clamping line direction (often also the transversal direction) direction may be limited. The constant curvature has shown to be obtained for both the transversal and the longitudinal direction. The situation can be visualised by placing the cantilever on a sphere. Since the surface stress changed is observed as a relative change in the resistance it has been found that both the transverse and longitudinal stress has to be considered, and furthermore, it has been found that they can be considered equally, irrespectively of the width and length of the piezoresistive material, when the cantilever is not subjected to other forces, such as a resistive force generated due to clamping. It has thus been found that an optimal signal or signal/noise ratio is obtained when the piezoresistive element is arranged so that the numerically value of the sum of the longitudinal piezoresistive coefficient π_l and the transverse piezoresistive coefficient π_t is at least (in 10^{-11} Pa^{-1}) $10 \times P$, such as $20 \times P$, such as $30 \times P$, such as $40 \times P$, wherein P is the piezoresistance factor.

Example 1

30

A simulation of the surface stress sensitivity for a cantilever with the following dimensions and as shown in figure 4, and with the piezoresistor placed in the $\langle 110 \rangle$

direction has been performed. In figure 4 the cantilever is seen in a sectional side view. The cantilever has a length of about 120 μm and a width of about 50 μm .

5

Cantilever Dimensions	Thickness [nm]	Young's modulus [GPa]	Pre-stress [MPa]
Au	30	80	40
SiN	45	200	85
Si	150	180	20
SiO ₂	100	70	-290
SiN	145	200	75

The single crystalline silicon piezoresistor was simulated with respectively, a p-type and an n-type resistor. The result is:

p-type

$$\frac{\Delta R}{R}/\sigma_x = 2.97 \cdot 10^{-4} (N/m)^{-1}$$

n-type

$$\frac{\Delta R}{R}/\sigma_x = -2.83 \cdot 10^{-3} (N/m)^{-1}$$

20

As seen from the simulation the sensitivity for an n-type single crystalline silicon piezoresistor used for

surface stress sensitivity is almost a factor of 10 more sensitive than a p-type single crystalline silicon piezoresistor.

5

Example 2

In order to exemplify the increase of sensitivity by using an n-type piezoresistive cantilever as a surface stress sensor instead of a p-type piezoresistive cantilever, an experiment that changes the surface stress in a controlled manner is performed.

An example of such an experiment is measuring the change in surface stress when the molecule Mercaptohexanol is immobilized to a gold layer on the topside of a cantilever surface. The immobilization of Mercaptohexanol is performed due to the binding between the -SH group in Mercaptohexanol and the gold layer. The immobilization of Mercaptohexanol is finalized when a complete monolayer is formed on the gold surface. Since the surface stress of the cantilever is changed during this procedure, this can be monitored as a change in signal from the piezoresistive cantilever. When the monolayer has been formed the signal will become constant. The amplitude of the signal is then defined as difference between the signal before the introduction of Mercaptohexanol and the signal from the piezoresistor after the Mercapothexanol monolayer is formed on the cantilever gold.

The experiment consists of observing the amplitude of two almost identical piezoresistive cantilevers, wherein the cantilevers differs in that one of the

piezoresistive cantilevers has incorporated an n-type piezoresistor while the other has a p-type piezoresistor. In this example the piezoresistors is placed in the <110> direction of the silicon crystal and
 5 P=1 for both n-type and p-type. The piezoresistors are inserted in a Wheatstone bridge as seen in figure 2. The change in output voltage from the Wheatstone bridge is given:

$$10 \quad \Delta V = \frac{1}{4} \frac{\Delta R}{R} \sigma_s \cdot V$$

Where ΔV is the output voltage and V is the input voltage, σ_s is the surface stress and $\Delta R/R$ is the relative change of resistance of the piezoresistor.
 15 Since the relative change in resistance is given by:

$$\frac{\Delta R}{R} = \pi_l \cdot \sigma_l + \pi_t \cdot \sigma_t$$

Where π_l and π_t are the piezoresistive coefficients in
 20 the longitudinal and transversal direction, respectively. σ_l and σ_t are the stress in the piezoresistive layer. It can be assumed that $\sigma_l = \sigma_t = \sigma$ and $\sigma_s \propto \sigma$.

25 Using the above considerations together with the piezoresistive coefficients in the table 1, the output voltage for a p-type piezoresistive cantilever can be written as:

$$30 \quad \Delta V_{p-type} \propto (\pi_l + \pi_t) \sigma_s \cdot V = 6 \cdot \sigma_s \cdot V$$

and for an n-type piezoresistor:

$$\Delta V_{n-type} \propto (\pi_l + \pi_t) \sigma_s \cdot V = -49 \cdot \sigma_s \cdot V$$

- 5 As it is seen from the two equations, there is a factor of about 8 in difference in sensitivity in favour of n-type piezoresistive cantilever, and the change in output voltage has opposite signs for the same surface stress.
- 10 In the experiment, the cantilevers are inserted in a micro liquid handling system as described in WO 0066266. The $V=2.5$ V is applied to the Wheatstone bridge (input voltage) and the signal from the Wheatstone bridge is monitored by a voltmeter. First, water is pumped through
- 15 the system in order to stabilize the system. Hereafter, 1 mM Mercaptohexanol is introduced in the micro liquid handling system and the signal starts to change. The graph in figure 3 is an example of such an experiment. It can be seen that the signal from the n-type
- 20 piezoresistive cantilever has a signal, which is about 8 times larger, and with opposite sign compared to the change in signal from the p-type piezoresistive cantilever.

25 **Example 3**

A cantilever as shown in figure 4 was provided. The gold was applied in the form of a film. During to the application of the gold film, the gold film was

30 stretched in all directions, so that cantilever surface after the release of the gold layer was subjected to a stress. The stress of the surface was determined by finite element simulation. In the cantilever surface shown in figure 5 the stress is indicated by the

white/grey/black colour. The darker the colour the higher is the stress that is measured. In areas 52 adjacent the clamping line 51 the bending in the clamping line direction is limited and accordingly the level of stress measured is less than longer away 53 from the clamping line. The rule of thumb is that the stress in both the transverse and longitudinal direction can be considered un-effected of the clamping when the distance X from the clamping is about $X > 0.25 \times W$ where W is the width of the cantilever.